High intensity interval and moderate intensity continuous training improves whole body insulin sensitivity and lowers muscle ceramide content in obese individuals

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Moderate intensity continuous (MICT) and high intensity interval training (HIT) have been shown to improve oxidative capacity, increase intramuscular lipid storage and utilisation, and increase the abundance of the lipid-droplet coating proteins perilipin 2 and perilipin 5 in skeletal muscle (Shepherd *et al*. 2013). Such improvements in muscle lipid handling may promote greater muscle insulin sensitivity by lowering the concentration of bioactive lipid species, such as diacylglycerol (DAG) and ceramides, which are known to antagonise muscle insulin signalling. The aim of the present study was to use a lipidomic approach to investigate the changes in muscle lipid composition following short term exercise training in obese males. We hypothesized that improvements in whole body insulin sensitivity following 4 weeks of HIT and MICT would be accompanied by reductions in skeletal muscle DAG and/or ceramide concentrations.

Sixteen sedentary obese males performed 4 weeks of either HIT (4-7x 30s sprints at 200% peak power output, 3 days per week) or MICT (40-60 min cycling at ~65% VO_{2peak}, 5 days per week). Maximal aerobic capacity ($VO_{2\ peak}$), oral glucose tolerance tests and muscle biopsies from the vastus lateralis were collected before the intervention and 48 h after the final exercise bout. Lipid analysis was performed by electrospray ionisation-tandem mass spectrometry.

In response to training, $VO_{2\ peak}$ was increased following both HIT and MICT (7±3% and 11±3% respectively; main training effect, $P < 0.01$) and the Matsuda index of insulin sensitivity improved to a similar extent following both interventions (HIT 12±5%, MICT 19±6%; main training effect, $P < 0.01$). No significant changes in total triacylglycerol (TAG) or DAG content or in specific DAG or TAG species were observed in response to training ($P > 0.05$). Training induced a significant reduction in total ceramide content (HIT -17±14%, MICT -16±7%; main training effect, $P = 0.03$), with a decrease in ceramide 24:0 ($P= 0.048$) and ceramide 18:0 ($P = 0.06$) species. Further, a significant increase in the total content of trihexosylceramide (THC) was detected in response to training (HIT 30±7%, MICT 13±12%; main training effect, $P = 0.03$), with specific increases in THC 24:0 and THC 24:1 species ($P < 0.01$). There were no changes in the total or species specific content of monohexosylceramide or dihexosylceramide in either group ($P > 0.05$). There were no significant differences in the training responses between MICT and HIT for any of the measured variables.

This study demonstrates that 4 weeks of MICT or HIT leads to comparable improvements in whole body oxidative capacity and insulin sensitivity. Further, this is the first study to demonstrate that both HIT and MICT can lower ceramide concentrations in skeletal muscle of obese males. As ceramide accumulation is intimately linked to obesity and skeletal muscle insulin resistance (Coen *et al.*, 2010), the changes in lipid composition following exercise training likely provide an intracellular environment which enhances muscle insulin sensitivity in obese males. This study offers new insight into the mechanisms by which MICT and HIT can improve muscle insulin sensitivity and further supports the effectiveness of HIT as an efficient means to improve metabolic health.

Shepherd SO, Cocks M, Tipton KD, Ranasinghe A, Barker T, Wagenmakers AJM, Shaw CS. (2013) Enhanced intramuscular triglyceride metabolism and improved insulin sensitivity in response to traditional endurance and high intensity interval training. *Journal of Physiology* **591**: 657-675.

Coen PM, Dube JJ, Amati F, Stefanovic-Racic M, Ferrell RE, Toledo FGS, Goodpaster BH. (2010) Insulin resistance is associated with higher intramyocellular triglycerides in type I but not type II myocytes conocomitant with higher ceramide content. *Diabetes* **59**: 80-88.